

CLAIMS

We claim:

1. A method for modulating the immunogenicity of a target protein, said method comprising:
5 a) inputting a protein backbone structure with variable residue positions of a target protein
 into a computer;
 b) computationally generating a set of primary variant amino acid sequences; and,
 c) applying a computational immunogenicity filter against said set to identify at least one
 candidate variant protein.

10 2. A method according to claim 1 further comprising testing said candidate variant protein to
 determine if said immunogenicity is altered relative to said target protein.

15 3. A method according to claim 1 further comprising classifying each variable residue position as
 either a core, surface or boundary residue.

20 4. A method according to claim 1 wherein said computationally generating step comprises a DEE
 computation.

25 5. A method according to claim 4 wherein said DEE computation is selected from the group
 consisting of original DEE and Goldstein DEE.

30 6. A method according to claim 1 wherein said set of primary variant amino acid sequences are
 optimized for at least one scoring function.

35 7. A method according to claim 6 wherein said set of primary variant amino sequences optimized for
 at least one scoring function comprises the globally optimal protein sequence.

30 8. A method according to claim 6 wherein said scoring function is selected from the group consisting
 of a Van der Waals potential scoring function, a hydrogen bond potential scoring function, an atomic
 salvation scoring function, an electrostatic scoring function and a secondary structure propensity
 scoring function.

35 9. A method according to claim 1 wherein said computationally generating step includes the use of a
 Monte Carlo search.

10. A method according to claim 1 wherein said target protein is from a non human species and said candidate variant protein exhibits reduced immunogenicity in humans.
- 5 11. A method according to claim 1 wherein the immunogenicity of said candidate variant protein is reduced relative to said target protein.
12. A method according to claim 1 wherein said candidate variant protein is non-immunogenic.
- 10 13. A method according to claim 11 or 12 wherein said candidate variant protein is more stable than said target protein.
14. A method according to claim 1 wherein said modulating the immunogenicity of said target protein comprises modifying the amino acid sequence that binds to an MHC molecule.
- 15 15. A method according to claim 14 wherein said MHC molecule belongs to MHC class I.
16. A ...od according to claim 14 wherein said MHC molecule belongs to MHC class II.
- 20 17. A method according to claim 1 wherein said modulating the immunogenicity of said target protein comprises modifying an amino acid sequence encoding a T cell epitope.
- 25 18. A method for modulating the immunogenicity of a target protein, said method comprising:
 a) inputting a protein backbone structure with variable residue positions of a target protein into a computer;
 b) applying a computational immunogenicity filter to identify at least one candidate variant protein;
 d) computationally analyzing said variant protein for maintenance of native fold and stability; and
 d) generating a set of primary variant amino acid sequences.

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